

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43bis.1)

To:

see form PCT/ISA/220

Date of mailing
(day/month/year) see form PCT/ISA/210 (second sheet)Applicant's or agent's file reference
see form PCT/ISA/220**FOR FURTHER ACTION**
See paragraph 2 belowInternational application No.
PCT/NL2005/000134International filing date (day/month/year)
23.02.2005Priority date (day/month/year)
23.02.2004International Patent Classification (IPC) or both national classification and IPC
INV. G06F19/00
ADD. C12Q1/68Applicant
ERASMUS UNIVERSITEIT ROTTERDAM

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA:



European Patent Office - P.B. 5818 Patentlaan 2
NL-2280 HV Rijswijk - Pays Bas
Tel. +31 70 340 - 2040 Tx: 31 651 epo nl
Fax: +31 70 340 - 3016

Date of completion of
this opinionsee form
PCT/ISA/210

Authorized Officer

Godzina, Przemyslaw

Telephone No. +31 70 340-3170



**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/NL2005/000134

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:
 - ☒ the international application in the language in which it was filed
 - ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1 (b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
 - a. type of material:
 - ☐ a sequence listing
 - ☐ table(s) related to the sequence listing
 - b. format of material:
 - ☐ on paper
 - ☐ in electronic form
 - c. time of filing/furnishing:
 - ☐ contained in the international application as filed.
 - ☐ filed together with the international application in electronic form.
 - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/NL2005/000134

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of

- ☐ the entire international application
- ☒ claims Nos. 10-21

because:

- ☒ the said international application, or the said claims Nos. 11 relate to the following subject matter which does not require an international search (*specify*):

see separate sheet

- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 10 are so unclear that no meaningful opinion could be formed (*specify*):

see separate sheet

- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed (*specify*):
- ☒ no international search report has been established for the whole application or for said claims Nos. 12-21
- ☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:
 - ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
 - ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
 - ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13ter.1(a) or (b).
- ☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-bis of the Administrative Instructions.
- ☐ See Supplemental Box for further details

**WRITTEN OPINION OF THE
INTERNATIONAL SEARCHING AUTHORITY**

International application No.
PCT/NL2005/000134

Box No. IV Lack of unity of invention

1. ☐ In response to the invitation (Form PCT/ISA/206) to pay additional fees, the applicant has, within the applicable time limit:
- ☐ paid additional fees
 - ☐ paid additional fees under protest and, where applicable, the protest fee
 - ☐ paid additional fees under protest but the applicable protest fee was not paid
 - ☐ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is
- ☐ complied with
 - ☒ not complied with for the following reasons:
see separate sheet
4. Consequently, this report has been established in respect of the following parts of the international application:
- ☐ all parts.
 - ☒ the parts relating to claims Nos. 1-11

Box No. V Reasoned statement under Rule 43b/s.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	
	No: Claims	1-9
Inventive step (IS)	Yes: Claims	
	No: Claims	1-9
Industrial applicability (IA)	Yes: Claims	1-9
	No: Claims	

2. Citations and explanations

see separate sheet

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

Independent claim 10

- 1 The present application does not meet the requirements of Article 17(2)(a)(ii) PCT, because the description does not provide support and disclosure in the sense of Article 6 and 5 PCT for a part of the subject-matter of claim 10. Indeed, the independent claim 10 relates to reference data obtainable from the Internet under URL <http://www.ncbi.nlm.nih.gov/geo>. However, due to the dynamic character of data collections being posted on the Internet there is no proof that data available under the above-mentioned URL address before or on the date of filing have not been modified after the date of filing. This non-compliance of the application with the substantive provisions is to such an extent, that it excludes the subject-matter of claim 10 from search (PCT Guidelines 9.26 and 9.27).

Independent claim 11

- 2 The present application does not meet the requirements of Article 17(2)(a)(i) PCT, because the subject-matter of claim 11 is an example of mere presentation of information (Rule 39.1(v) PCT). Indeed, the subject-matter of independent claim 11 discloses a classification scheme for acute myeloid leukemia (AML) comprising a plurality of distinct AML classes. Such a classification scheme is considered as a disembodied data structure that has no interaction with a computational method for producing a classification scheme for AML. Thus, the content of claim 11 is nothing but mere arrangement of data what makes its subject-matter excluded from search (PCT Guidelines 9.11).

Re Item IV

Lack of unity of invention

- 1 Reference is made to the following document:

- D1: Tibshirani R. *et al.* (2002) "Diagnosis of multiple cancer types by shrunken centroids of gene expression", Proceedings of the National Academy of Sciences of USA, vol. 99, no. 10, pages 6567-6572
- 2 This Authority considers that there are two inventions covered by the claims indicated as follows:

I: Claims 1-11

directed to a computational method for producing a classification scheme for acute myeloid leukemia; a classification scheme generated by the said method; a method for classifying acute myeloid leukemia of an acute myeloid leukemia affected subject based on the said classification scheme; a method for diagnosing acute myeloid leukemia in a subject based on the said classification scheme; and a method of determining a prognosis for an acute myeloid leukemia affected subject based on the said classification scheme.

II: Claims 12-21

directed to an experimental method, applying oligonucleotide probes, oligonucleotide microarrays and kits-of-parts, for detecting an acute myeloid leukemia-associated transcript in a cell.

The reasons for which the inventions are not so linked as to form a single general inventive concept, as required by Rule 13.1 PCT, are as follows:

For the following reasoning the prior art as described in document D1 is taken into consideration.

From the comparison of the first invention (claims 1-11) and this prior art the following technical feature of the first invention can be seen to make a contribution and is, therefore, considered to be the special technical feature (Rule 13.2 PCT) of the first invention: methodological details of computationally producing a classification scheme for acute myeloid leukemia.

Following the same reasoning, comparing claims 12-21 and this same prior art, the

special technical feature of the second invention is: experimentally detecting, using oligonucleotide probes, oligonucleotide microarrays and kits-of-parts, an acute myeloid leukemia-associated transcript in a cell.

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1 Reference is made to the following documents:

- D1: Tibshirani R. *et al.* (2002) "Diagnosis of multiple cancer types by shrunken centroids of gene expression", Proceedings of the National Academy of Sciences of USA, vol. 99, no. 10, pages 6567-6572
- D2: EP-A-1 043 676
- D3: Ringnér M. *et al.* (2002) "Analyzing array data using supervised methods", Pharmacogenomics, vol. 3, no. 3, pages 403-415

2 The present application does not meet the criteria of Article 33(1) PCT, because the subject-matter of claims 1-9 is neither new nor inventive in the sense of Article 33(2) and 33(3) PCT, respectively.

Independent claim 1

2.1 The document D2 discloses (the references in parentheses applying to this document):

A method for producing a classification scheme for AML (paragraph [0005], l. 39-46) comprising the steps of:

- a) providing a plurality of reference samples, said reference samples comprising cell samples from a plurality of reference subjects affected by AML (claim 25);
- b) providing reference profiles by establishing a gene expression profile for each of said reference samples individually (claim 25);
- c) clustering said individual reference profiles according to a statistical procedure, comprising:

- (i) K-means clustering (paragraph [0068]);
- (ii) hierarchical clustering (paragraph [0068]); and
- (iii) Pearson correlation coefficient analysis (paragraph [0047]); and
- d) assigning an AML class to each cluster (paragraph [0009], l. 40-43).

Therefore, the subject-matter of claim 1 is not new (Art. 33(2) PCT).

Dependent claims 2-9

2.2 Dependent claims 2-9 do not contain any features which, in combination with the features of any claim to which they refer, meet the requirements of the PCT in respect of novelty (Art. 33(2) PCT) and/or inventive step (Art. 33(3) PCT), see documents D1-D3 and the corresponding passages cited in the search report.